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Laparoscopic Splenectomies for Idiopathic Thrombocytopenic Purpura: Experience of Sixty Cases

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We performed a laparoscopic splenectomy (LS) in 60 patients (age 9–83, 45 females) with idiopathic thrombocytopenic purpura (ITP) who did not achieve sustained remission on steroid therapy. Using a modified procedure, the mean duration of LS was 78 min (range 25–240 min) and surgery was associated with only 5% major and 5% minor complications. Ten patients had a platelet count less than 50 × 10^9/l during surgery despite the administration of immune globulin (0.4 g/kg × 3–5 days) or pulsed oral dexamethasone (40 mg/day × 4 days). Three patients were refractory to these therapies and underwent LS with a platelet count less than 5 × 10^9/l. Bleeding complications during or after surgery were rare (5%). Accessory spleens were removed in eight patients. Convalescence was rapid and the mean hospital stay was 2.3 days (range 1–7 days). The patients were followed for a mean of 16 months (range 1–36 months), and 49 patients (84%) are in complete remission. Seven patients (12.5%) relapsed despite an initial good response in 6 of them. Two patients underwent laparoscopic removal of accessory spleens with excellent response. We conclude that LS for ITP is safe and effective and associated with low morbidity and fast recovery. Thus, LS may be considered earlier in the course of ITP. Am. J. Hematol. 63:7–10, 2000.

Key words: laparoscopic splenectomy (LS); idiopathic thrombocytopenic purpura (ITP)

INTRODUCTION

Splenectomy is an effective therapeutic modality for the treatment of idiopathic thrombocytopenic purpura (ITP). Following this surgery, 70% of patients will achieve a prolonged complete response [1–3]. However, many patients who fail medical treatment are either not referred for operation or present relatively late in terms of optimal benefit from surgical intervention. This is mainly because of the possible complications associated with conventional splenectomy (CS), which include pulmonary atelectasis, subphrenic infections, and wound complications, all of which appear at rates as high as 20–25% of the patients [4–6].

Application of laparoscopic techniques for splenectomy was first reported in 1992 [7]. Since then, several retrospective studies have demonstrated that laparoscopic splenectomy (LS) is feasible and safe, and LS is associated with lower morbidity rates and faster recovery time compared to the CS [6,8–10]. However, the number of ITP patients, who underwent LS and were included in these studies, was small, and the patients were operated for various other indications as well. Long-term follow-ups were not reported.

We report our recent experience with 60 patients who underwent laparoscopic splenectomy because of nonresponsive or refractory ITP. The patients were followed up prospectively for up to 36 months after surgery.

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PATIENTS AND METHODS

ITP was diagnosed according to the guidelines of the American Society of Hematology [11]. All patients underwent bone marrow aspiration and other causes of thrombocytopenia were ruled out. Indications for surgery were as follows: resistant thrombocytopenia following treatment with steroids and/or intravenous immunoglobulins (IVIG) infusion, steroid-dependent disease, and recurrent thrombocytopenia following a remission achieved with adequate steroid therapy. All patients were scheduled for LS because this is now the usual surgical approach in our hospital.

Surgery

Preparation. The patients were given a polyvalent pneumoccocal vaccine (Pasteur Merieux, Lyon, France) at least 2 weeks before surgery. Prior to surgery the patients received either IVIG (Sandoglobulin, 0.4 g/kg/day for 5 days), or pulsed oral high-dose dexamethasone (40 mg/day, for 4 days).

Operative technique. The patient is anesthetized and a nasogastric tube is placed. The first five patients were operated in a supine position, and the other patients are now placed in the right lateral position with the table slightly extended in order to enlarge the space between the costal margin and the iliac crest [12]. This position allows a good visualization of the operative field with almost no need for any further retraction, and a very good exposure of the short gastric vessels is achieved. The procedure is performed through 5–10 mm incisions. The abdomen is insufflated with CO_2, and three laparoscopic ports are introduced to allow a laparoscope and surgical instruments into the abdominal cavity. The procedure is started by a thorough search for accessory spleens. Then, the splenic flexure of the colon is dissected down using coagulating scissors. After the anterior aspect of the hilum is exposed, the left gutter is dissected and the spleen is separated from the kidney and the diaphragm, except for the last posterior attachments of the upper pole. At this point, the spleen remains attached almost only by the vascular supply and the gap between the splenic hilum and tail of the pancreas is enlarged. The spleen is now lifted and an endoscopic stapling device is used to divide the hilum. This usually requires one or two applications of the instrument, and an additional application is used to divide the short gastric vessels. The last attachments to the diaphragm are incised with coagulating scissors. The spleen is then placed in a plastic bag, the opening of which is delivered out through the most lateral port. The opening of the bag is held and the spleen is crushed using a regular ring clamp with the additional use of a powerful suction device. After the spleen is withdrawn, the operative field is irrigated with lactated Ringer's solution, and another inspection for bleeding and a missed accessory spleen is made. At the end of the procedure the nasogastric tube is removed.

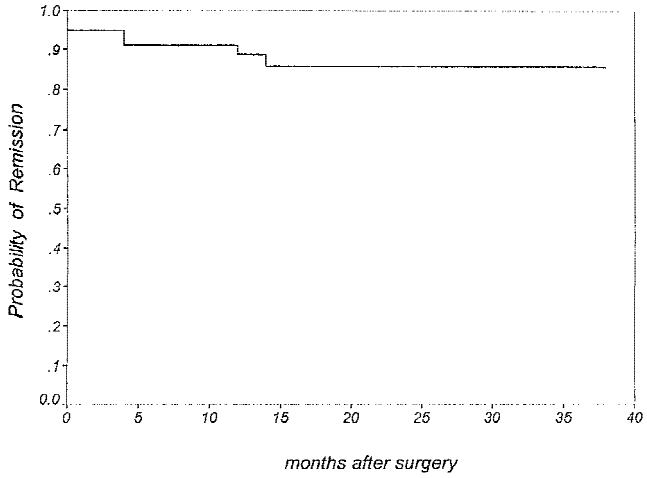

Fig. 1. Kaplan–Meier analysis of the remission rate (i.e., platelet count >50 × 10^9 without treatment) in 60 ITP patients following laparoscopic splenectomy.

Statistics

A Kaplan–Meier curve was used to estimate the probability of remission without a significant thrombocytopenia (<50 × 10^9/l) requiring additional therapy (Fig. 1).

RESULTS

Sixty ITP patients underwent laparoscopic splenectomy between April 1995 and March 1998. Their mean age was 34 years (range, 9–83), and 45 were female. The mean time from diagnosis was 33 months (range, 1–240). Thirty-three patients (55%) underwent splenectomy because of steroid failure following an initial good response to oral prednisone (1 mg/kg/day) or following two or more courses of pulsed oral high-dose dexamethasone. Nine patients (15%) needed chronic prednisone treatment in order to maintain an adequate platelet count. Eighteen patients (30%) were resistant to steroids; of these, 12 were treated with IVIG but only transient elevation of their platelet counts was observed.

Prior to surgery, 48 patients received pulsed oral dexamethasone and 12 received IVIG. At the time of surgery, 28 patients (47%) had a platelet count over 100 × 10^9/l, in 19 (35%) it was 50–100 × 10^9/l, and in 10 (l6.6%) it was 20–50 × 10^9/l. The three remaining patients were refractory to the above treatments and had less than 5 × 10^9/l. They received a platelet transfusion prior to surgery (12 units of random donor platelets). The platelet count of one of them rose to 24 × 10^9/l, but the other two had no response and were operated with a platelet count of 3 × 10^9/l. Excessive bleeding during surgery was rare, occurring in only two patients whose platelet counts dur-

ing the operation were 3×10^9/l and 20×10^9/l. A platelet transfusion was given to both patients, with no increment of their platelet count.

Three other patients received 1–2 units of packed red blood cells. Accessory spleens were found and removed in eight patients (13.5%). One of these patients had two accessory spleens. The procedure was concluded laparoscopically in all patients. The mean operating time was 78 min (range, 25–240). There were three (5%) major postoperative complications: a subphrenic abscess, which required percutaneous drainage in two patients, and deep vein thrombosis in one patient. Three patients (5%) had minor complications, including minor pulmonary atelectasis, a wound infection, and urinary retention, all of which resolved with appropriate treatment. The mean hospital stay was 2.3 days (range, 1–7). On the average, oral intake was begun within 24 h from surgery. All patients reported a rapid convalescence period with return to normal activities within 10 days after surgery.

Fifty-eight patients (96.6%) were available for a mean follow up of 16 months (range, 1–36), and 38 patients were followed for a period exceeding 16 months. At the time of this writing, 49 patients (84%) are in complete remission with a platelet count of over 100×10^9/l. Two patients (3.5%) are in a stable partial remission with a platelet count of $50–100 \times 10^9$/l and receive no therapy.

Seven patients (12.5%) developed recurrent thrombocytopenia requiring treatment (including low-dose steroids, danazol, and vitamin C), of whom 6 had an initial response to surgery with a significant rise of their platelet count ($>100 \times 10^9$/l). From these six patients: in two, the thrombocytopenia recurred within a few weeks and in the other four it recurred 4 (2 patients), 12, and 14 months after surgery (Fig. 1). Only one patient had no immediate elevation of her platelet counts after surgery. This patient underwent the operation with a platelet count of 3×10^9/l and was refractory to any preoperative treatment. She had no excessive bleeding during surgery and postoperatively received danazol, prednisone, vitamin C, colchicine, and tamoxifen. Currently, 6 months after the operation, she has a platelet count of 42×10^9/l without any hemorrhagic tendency. The three patients with early relapse were women, and two of them were found to have anticardiolipin antibodies but no other positive tests for systemic lupus erythematosus. The seven patients who had recurrent thrombocytopenia underwent three-dimensional scanning (SPECT) with radioactively labeled heat-damaged red blood cells. Accessory spleens were found in two patients and were removed laparoscopically with a good, lasting response.

These two patients had their recurrence 4 months after the operation, and until the recurrence had normal platelets count. The second procedure was done 6 months after the first one. The accessory spleens were 8 and 5 mm in size. One elderly patient (83 years old) died of an unrelated cause (acute myocardial infarction) 12 months after LS.

During the study period, an additional 20 LS were performed for indications other than ITP, including 4 patients with relapsing thrombotic thrombocytopenic purpura, 6 with hereditary spherocytosis, 4 with autoimmune hemolytic anemia, 3 with splenic lymphoma, and 3 with chronic lymphocytic leukemia. The periopertive complications in this group were also minimal, and all patients were discharged from the hospital and resumed normal activities within few days.

DISCUSSION

Our study demonstrates that laparoscopic splenectomy is a safe and efficacious procedure in ITP patients in whom elective splenectomy is indicated. The modified technique which we now use, i.e., the right lateral positioning of the patients and the en-masse division of the splenic vasculature using the laparoscopic stapler, decreased the postoperative morbidity and the operating time.

It is difficult to compare the outcome of LS to the results of conventional splenectomy. Most previous reports on conventional splenectomy were retrospective and collected over a long period of time and failed to follow the patients systematically and prospectively. In specializing centers, LS has become the procedure most commonly performed for elective splenectomy, making a randomized study very difficult to perform. Several studies tried to compare their results of LS to historical results of CS [6,10,13]. Two of them [6,10] demonstrated that LS carried a similar complication rate as CS: a total of 20–25%, of which 10% were minor complications, such as pulmonary atelectasis, and 10–15% were major complications which required medical intervention or reoperation. A recent large study of LS, 64 cases with various hematological disorders [14], showed a complication rate of 16% similar to the 10% complication rate observed in our patients. The low complication rate could be attributed to several factors: accumulation of surgical experience, the development of a standardized surgical procedure minimizing vascular injury associated with conversion to an open procedure [10,15], and the small size of the spleen in ITP, which makes LS less technically difficult [10,16]. Another reason for the low complication rate is the lack of patients with HIV, which contributes substantial morbidity and even mortality [9,14]. The mean operating time in our patients (78 min) was significantly shorter compared to the median length of the operation reported by others (170 min) [6,8,9]. This may also be related to the accumulated experience of the surgeon [10,13,17].

LS carries additional advantages including: reduced operative trauma; less splenosis and better detection of

accessory spleens; less post-operative pain; cosmetic advantage (important to young females, who comprise the majority of the cases); early discharge, mostly within 48 h after surgery and the ability to resume normal activity within a few days. These advantages compensate for the use of expensive laparoscopic instruments making the total cost of the procedure comparable or even cheaper than CS [9,17].

One reason for recurrence of ITP postsplenectomy may be an accessory spleen that is missed during the operation. The 14% total rate of accessory spleens which were discovered during LS in our patients is comparable to the rate of 15–18% reported in patients with ITP who underwent CS [4,18]. LS allows a good exploration of the most common locations for accessory spleens which include the: splenic hilum, tail of the pancreas, the splenocolic and gastrosplenic ligaments, and the greater omentum. Therefore, a thorough search for the accessory spleen is critically important. Despite such precautions, two of our patients with postsurgical recurrence of ITP were found to have accessory spleens which were removed successfully by an additional laparoscopic procedure.

Another possible reason for surgical failure is splenic injury with subsequent splenosis [19]. During surgery, the spleen should be handled with great care to avoid fragmentation and spillage of tissue. In a recent study, a very high incidence (9 out of 18) of residual splenic tissue detected on routine postoperative scintigraphy after laparoscopic splenectomy was reported [20]. In that study, 3 of the 9 patients with residual splenic tissue had signs of disease recurrence. In our group, none of the patients who had recurrent ITP had splenosis, but neither we nor others searched for residual splenic tissue in the absence of clinical signs. The clinical significance of accessory or residual splenic tissue and the relation between their presence and recurrent thrombocytopenia remains unknown.

The results we report in the ITP patients who had a lasting response of 88% are gratifying compared to the acceptable remission rate of 70% [1–3,18]. Only seven patients developed a recurrent disease, which required treatment, and two others had a partial remission without the need for treatment. The high response rate cannot be due to patients selection, since the mean preoperative duration of the ITP was rather long (33 months), and various therapeutic modalities were tried prior to LS in the majority of the patients. What may have improved the results is the careful dissection needed for performing and concluding the laparoscopic procedure. Thus, the spleen is almost always removed intact, with no vascular or capsular injury resulting in a significantly lower rate of splenosis. Also, accessory spleen are easily recognized and removed.

We conclude that LS is safe and effective for the treatment of ITP and may yield better results compared to CS. It should be performed as the procedure of choice for elective splenectomy, and may be considered earlier in the course of ITP.

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